Table 1 is 23 amino acids in length and thus, is 2 amino acids longer than an amino acid sequence which encompasses amino acid residue 630 through amino acid residue 650 of the HER-2 protein. Thus, the amendment adds no new matter.

Applicant is also submitting herewith a substitute Sequence Listing and a computer readable form of the paper copy of the substitute Sequence Listing. The substitute Sequence Listing on the paper copy and CFR enclosed herewith are the same. The substitute Sequence Listing is the same as the original Sequence Listings filed with the Patent Office on April 9, 2001, November 21, 2001, and April 1, 2002 except that the substitute Sequence Listing contains one additional sequence, i.e., SEQ ID NO. 42. SEQ ID NO. 42 is the sequence which encompasses amino acid 628 through amino acid 647 of the HER-2 protein. Support for SEQ ID NO. 42 is found in corrected Table 1 of the specification and on page 12, lines 8 and 13 of the specification which refer to using a chimeric peptide which comprises a HER-2 B cell epitope comprising amino acid 628-647 of the HER-2 protein to invoke an antibody response in rabbits and to retard tumor development in mice. Thus, the SEQ ID NO. 42 adds no new matter to the application.

By the present amendment, Applicants have also amended claims 1, 3, 4, 5, 6, 9, 13, 14, 18, 21, and 22 for clarity. Support for the amendment to claim 1 is found in original claim 2 and on page 3, line 12-14 of the specification. Claims 3, 4, 5, 13, and 14 have been amended to depend from a different claim. Claim 6 has been amended to be independent. Support for the amendments to claim 6 is found in original claim 1 and on page 3, lines 12-14 of the specification. Support for the amendment to claim 9 is found in original claim 19, and on page 5, lines 17-18 of the specification. Claim 18 is amended to be independent; support for such amendment is found in original claim 9. Support for the amendment to claim 21 is found in original claims 1, 2, 9, 10, and 21. Support for the amendment to claim 22 is found in original claims 23 and 24. The amendments to the claims add no new matter.

By the present amendment, applicants have canceled claims 2, 10, 23, and 24 without prejudice or disclaimer. Applicants have also added claims 31-33. Support for new claim 31 is found on 19, lines 9-11. Support for new claims 32 and 33 is found on page 18, lines 4-10, and page 19, lines 5-12. Thus, new claims 31-33 add no new matter.

A document entitled "VERSION WITH MARKINGS TO SHOW CHANGES MADE" showing the additions as underlined and the deletions in brackets is attached hereto.

Applicant respectfully requests entry of the present Preliminary Amendment and the Substitute Sequence Listing.

Respectfully submitted,

Date: April 3, 2012

by: Pamela A. Docherty

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Page 11, line 1

Table 1. Consolidated Human p185 HER-2 predicted B cell epitopes listed in the order of ranking by amino acid residue numbers. Asparagine (N)-linked glycosylation sites are underlined in bold.

Predictive Ranking	Residue	Amino Acid Sequence	Secondary Structure
7	27 – 45	Tgtdmklrlpaspethldm	25 – 28 β turn; 29 – 32 α helix; 35 – 38 β turn
8 (DW5)	115 – 136	AVLDNGDPL**NNTT**PVTGASPGG	116 – 135 β turn
9	168 – 189	LWKDIFHKNNQLALTLIDT**NRS**	173 – 176 β turn; 177 – 181 α helix
1	182 – 216	TLIDT**NRSR**ACHPCSPMCKGSRCWG ESSEDCQSLT	184 – 212 β turn/loop
6	270 – 290	ALVTYNTDTFESMPNPEGRYT	273 – 286 β turn; 278 – 280 α helix
3	316 – 339	PLHNQEVTAEDGTQRAEKCSKPCA	319 – 324 α helix; 324 – 336 β turn.
10 (DW1)	376 – 395	PESFDGDPASNTAPLQPE	379 – 388 β turn
12 (DW6)	410-429	LYISAWPDSLPDLSVFQNLQ	413-421β turn
2	485 – 503	LFRNPHQALLHTANRPEDE	497 – 500 β turn; 499 – 504 α helix
11	560 – 593	CLPCHPECQPQ**NGSV**TCFGPEADQCVACAH YKDP	561 – 572 & 589 – 593 β turn; 579 – 581 α helix
4	605– 622	KPDLSYMPIWKFPDEEGA	616 – 620 α helix
5 (DW4)	[630] 628 – 650	ING*T*HSCVDLDDKGCPAEQRASP	635 – 642 β turn; 643 – 646 α helix

IN THE CLAIMS:

1. (Once Amended) A composition for stimulating an immune response to HER-2 protein, wherein said composition is a chimeric peptide and comprises [comprising] a HER-2 B cell epitope, a T helper (Th) epitope, and a linker joining said HER-B cell epitope to said Th epitope; said HER-2 B cell epitope being from 15 to 40 amino acids in length and comprising a sequence selected from the group consisting of:

TGTDMKLRLPASPETHLDM, SEQ ID NO. 1, or a functional equivalent thereof;

[AVLDNGDPLNNTTPVTGASPGG, SEQ ID NO. 2, or a functional equivalent thereof;
LWKDIFHKNNQLALTLIDTNRS, SEQ ID NO. 3, or a functional equivalent thereof;]
TLIDTNRSRACHPCSPMCKGSRCWGESSEDCQSLT, SEQ ID NO. 4, or a functional equivalent thereof;
ALVTYNTDTFESMPNPEGRYT, SEQ ID NO. 5, or a functional equivalent thereof;
PLHNQEVTAEDGTQRAEKCSKPCA, SEQ ID NO. 6, or a functional equivalent thereof;
[PESFDGDPASNTAPLQPE, SEQ ID NO. 7, or a functional equivalent thereof;
LYISAWPDSLPDLSVFQNLQ, SEQ ID NO. 8, or a functional equivalent thereof;]
LFRNPHQALLHTANRPEDE, SEQ ID NO. 9, or a functional equivalent thereof;
CLPCHPECQPQNGSVTCFGPEADQCVACAHYKDP, SEQ ID NO. 10, or a functional equivalent thereof; and
KPDLSYMPIWKFPDEEGA, SEQ ID NO. 11, or a functional equivalent thereof[; and
INGTHSCVDLDDKGCPAEQRAS, SEQ ID NO. 12, or a functional equivalent thereof].

3. (Once Amended) The composition of claim [2] 1 wherein [the HER-2 B cell epitope is from 15 to 50 amino acids in length, wherein] the Th epitope is a promiscuous Th epitope of from 14 to 22 amino acids in length, and wherein said linker is from 1 to 15 amino acids in length.

4. (Once Amended) The composition of claim [2] 1 wherein the Th epitope comprises a sequence selected from the group consisting of:
N-S-V-D-D-A-L-I-N-S-T-I-Y-S-Y-F-P-S-V, SEQ. ID. NO. 13, or a functional equivalent thereof;
P-G-I-N-G-K-A-I-H-L-V-N-N-Q-S-S-E, SEQ ID NO. 14, or a functional equivalent ther eof;
Q-Y-I-K-A-N-S-K-F-I-G-I-T-E-L, SEQ ID NO. 15, or a functional equivalent thereof;
F-N-N-F-T-V-S-F-W-L-R-V-P-K-V-S-A-S-H-L-E, SEQ ID NO. 16, or a functional equivalent thereof;
L-S-E-I-K-G-V-I-V-H-R-L-E-G-V, SEQ ID NO. 17, or a functional equivalent thereof;
F-F-L-L-T-R-I-L-T-I-P-Q-S-L-N, SEQ ID NO. 18, or a functional equivalent thereof; and
T-C-G-V-G-V-R-V-R-S-R-V-N-A-A-N-K-K-P-E, SEQ ID NO. 19, or a functional equivalent thereof.

5. (Once Amended) The composition of claim [2] 1 wherein the linker comprises the sequence GPSL, SEQ ID NO. 20.

6. (Once Amended) [The composition of claim 1] A composition for stimulating an immune response to HER-2 protein, wherein said composition is a multivalent peptide and comprises 2 or more HER-2 B cell epitopes, a Th cell epitope, and a template;

wherein said 2 or more HER-2 B cell epitopes are different, and wherein each of said 2 or or more HER-2 B cell epitopes is from 15 to 40 amino acids in length and comprises a sequence selected from the group consisting of:

TGTDMKLRLPASPETHLDM, SEQ ID NO. 1, or a functional equivalent thereof;

AVLDNGDPLNNTTPVTGASPGG, SEQ ID NO. 2, or a functional equivalent thereof;

LWKDIFHKNNQLALTLIDTNRS, SEQ ID NO. 3, or a functional equivalent thereof;

TLIDTNRSRACHPCSPMCKGSRCWGESSEDCQSLT, SEQ ID NO. 4, or a functional equivalent thereof;

ALVTYNTDTFESMPNPEGRYT, SEQ ID NO. 5, or a functional equivalent thereof;

PLHNQEVTAEDGTQRAEKCSKPCA, SEQ ID NO. 6, or a functional equivalent thereof;

PESFDGDPASNTAPLQPE, SEQ ID NO. 7, or a functional equivalent thereof;

LYISAWPDSLPDLSVFQNLQ, SEQ ID NO. 8, or a functional equivalent thereof;

LFRNPHQALLHTANRPEDE, SEQ ID NO. 9, or a functional equivalent thereof;

CLPCHPECQPQNGSVTCFGPEADQCVACAHYKDP, SEQ ID NO. 10, or a functional equivalent thereof;

KPDLSYMPIWKFPDEEGA, SEQ ID NO. 11, or a functional equivalent thereof; and

INGTHSCVDLDDKGCPAEQRAS, SEQ ID NO. 12, or a functional equivalent thereof; and

wherein the HER-2 B cell epitopes and the Th cell epitope are attached to the template.

9. (Once Amended) A composition for stimulating an immune response to HER-2 protein, wherein said composition is a chimeric peptide and comprises [comprising] a HER-2 CTL epitope, a T helper (Th) epitope; and a linker joining said HER-2 CTL epitope to said Th epitope;

said HER-2 CTL epitope being from 8 to 12 amino acids in length and comprising a sequence selected from the group consisting of:

ILWKDIFHK, SEQ ID. NO. 21; or a functional equivalent thereof;
ILKETELRK, SEQ ID. NO. 22; or a functional equivalent thereof;
VLRENTSPK, SEQ ID. NO. 23; or a functional equivalent thereof;
AARPAGATL, SEQ ID. NO. 24; or a functional equivalent thereof;
LPASPETHL, SEQ ID. NO. 25; or a functional equivalent thereof;
LPTHDPSPL, SEQ ID. NO. 26; or a functional equivalent thereof;
CRWGLLLAL, SEQ ID. NO. 27; or a functional equivalent thereof;
RRFTHQSDV, SEQ ID. NO. 28; or a functional equivalent thereof;
GRILHNGAY, SEQ ID. NO. 29; or a functional equivalent thereof;
TYLPTNASL, SEQ ID. NO. 30; or a functional equivalent thereof;
EYVNARHCL, SEQ ID. NO. 31; or a functional equivalent thereof;
AYSLTLQGL, SEQ ID. NO. 32; or a functional equivalent thereof;
ALCRWGLLL, SEQ ID. NO. 33; or a functional equivalent thereof;
HLYQGCQV, SEQ ID. NO. 34; or a functional equivalent thereof;
QLRSLTEIL, SEQ ID. NO. 35, or a functional equivalent thereof;
ILHNGAYSL, SEQ ID. NO. 36; or a functional equivalent thereof;
ILLVVVLGV, SEQ ID. NO. 37; or a functional equivalent thereof;
DLTSTVQLV, SEQ ID. NO. 38; or a functional equivalent thereof;
VLVKSPNHV, SEQ ID. NO. 39; or a functional equivalent thereof;
KIFGSLAFL, SEQ ID. NO. 40; or a functional equivalent thereof; and
IISAVVGIL, SEQ ID. NO. 41; or a functional equivalent thereof.

13. (Once Amended) The composition of claim [10] 9 wherein the Th epitope comprises a sequence selected from the group consisting of:
N-S-V-D-D-A-L-I-N-S-T-I-Y-S-Y-F-P-S-V , SEQ. ID. NO. 13, or a functional equivalent thereof;
P-G-I-N-G-K-A-I-H-L-V-N-N-Q-S-S-E, SEQ ID NO. 14, or a functional equivalent thereof;
Q-Y-I-K-A-N-S-K-F-I-G-I-T-E-L, SEQ ID NO. 15, or a functional equivalent thereof;
F-N-N-F-T-V-S-F-W-L-R-V-P-K-V-S-A-S-H-L-E, SEQ ID NO. 16, or a functional equivalent thereof;
L-S-E-I-K-G-V-I-V-H-R-L-E-G-V, SEQ ID NO. 17, or a functional equivalent thereof;
F-F-L-L-T-R-I-L-T-I-P-Q-S-L-N, SEQ ID NO. 18, , or a functional equivalent thereof; and

T-C-G-V-G-V-R-V-R-S-R-V-N-A-A-N-K-K-P-E, SEQ ID NO. 19, or a functional equivalent thereof.

14. (Once Amended) The composition of claim [10] 9 wherein the linker comprises the sequence GPSL, SEQ ID NO. 20.

18. (Once Amended) A [The] composition [of claim 9] for stimulating an immune response to a HER-2 protein, wherein said composition is a multivalent peptide and comprises 2 or more HER-2 CTL cell epitopes, a Th cell epitope, and a template;
wherein said 2 or more HER-2 CTL epitopes are different, and wherein each of said 2 or more HER-2 CTL epitopes comprises a sequence selected from the group consisting of:
ILWKDIFHK, SEQ ID. NO. 21; or a functional equivalent thereof;
ILKETELRK, SEQ ID. NO. 22; or a functional equivalent thereof;
VLRENTSPK, SEQ ID. NO. 23; or a functional equivalent thereof;
AARPAGATL, SEQ ID. NO. 24; or a functional equivalent thereof;
LPASPETHL, SEQ ID. NO. 25; or a functional equivalent thereof;
LPTHDPSPL, SEQ ID. NO. 26; or a functional equivalent thereof;
CRWGLLLAL, SEQ ID. NO. 27; or a functional equivalent thereof;
RRFTHQSDV, SEQ ID. NO. 28; or a functional equivalent thereof;
GRILHNGAY, SEQ ID. NO. 29; or a functional equivalent thereof;
TYLPTNASL, SEQ ID. NO. 30; or a functional equivalent thereof;
EYVNARHCL, SEQ ID. NO. 31; or a functional equivalent thereof;
AYSLTLQGL, SEQ ID. NO. 32; or a functional equivalent thereof;
ALCRWGLLL, SEQ ID. NO. 33; or a functional equivalent thereof;
HLYQGCQV, SEQ ID. NO. 34; or a functional equivalent thereof;
QLRSLTEIL, SEQ ID. NO. 35, or a functional equivalent thereof;
ILHNGAYSL, SEQ ID. NO. 36; or a functional equivalent thereof;
ILLVVVLGV, SEQ ID. NO. 37; or a functional equivalent thereof;
DLTSTVQLV, SEQ ID. NO. 38; or a functional equivalent thereof;
VLVKSPNHV, SEQ ID. NO. 39; or a functional equivalent thereof;
KIFGSLAFL, SEQ ID. NO. 40; or a functional equivalent thereof; and
IISAVVGIL, SEQ ID. NO. 41; or a functional equivalent thereof; and

wherein the HER-2 CTL epitopes and the Th cell epitope are attached to the template.

21. (Once Amended) A method of stimulating an immune response in a subject comprising administering to said subject a [composition] chimeric peptide selected from the group consisting of [the composition] a chimeric peptide of claim 1, [the composition] a chimeric peptide of claim 9, and [a polypeptide which comprises the composition of claim 1 and the composition of claim 9] and c) a chimeric peptide which comprises one or more HER-2 B cell epitopes, one or more HER-2 CTL epitopes, a Th epitope and a linker linking said one or more HER-2 B cell epitopes and said one or more HER-2 CTL epitopes to said Th epitope;

wherein each of said one or more HER-2 B cell epitope comprises a sequence selected from the group consisting of

TGTDMKLRLPASPETHLDM, SEQ ID NO. 1, or a functional equivalent thereof;

AVLDNGDPLNNTTPVTGASPGG, SEQ ID NO. 2, or a functional equivalent thereof;

LWKDIFHKNNQLALTLIDTNRS, SEQ ID NO. 3, or a functional equivalent thereof;

TLIDTNRSRACHPCSPMCKGSRCWGESSEDCQSLT, SEQ ID NO. 4, or a functional equivalent thereof;

ALVTYNTDTFESMPNPEGRYT, SEQ ID NO. 5, or a functional equivalent thereof;

PLHNQEVTAEDGTQRAEKCSKPCA, SEQ ID NO. 6, or a functional equivalent thereof;

PESFDGDPASNTAPLQPE, SEQ ID NO. 7, or a functional equivalent thereof;

LYISAWPDSLPDLSVFQNLQ, SEQ ID NO. 8, or a functional equivalent thereof;

LFRNPHQALLHTANRPEDE, SEQ ID NO. 9, or a functional equivalent thereof;

CLPCHPECQPQNGSVTCFGPEADQCVACAHYKDP, SEQ ID NO. 10, or a functional equivalent thereof;

KPDLSYMPIWKFPDEEGA, SEQ ID NO. 11, or a functional equivalent thereof; and

INGTHSCVDLDDKGCPAEQRAS, SEQ ID NO. 12, or a functional equivalent thereof;

wherein each of said one or more HER-2 CTL epitope comprises a sequence selected from the group consisting of

ILWKDIFHK, SEQ ID. NO. 21; or a functional equivalent thereof;

ILKETELRK, SEQ ID. NO. 22; or a functional equivalent thereof;

VLRENTSPK, SEQ ID. NO. 23; or a functional equivalent thereof;

AARPAGATL, SEQ ID. NO. 24; or a functional equivalent thereof;

LPASPETHL, SEQ ID. NO. 25; or a functional equivalent thereof;

LPTHDPSPL, SEQ ID. NO. 26; or a functional equivalent thereof;

CRWGLLLAL, SEQ ID. NO. 27; or a functional equivalent thereof;
RRFTHQSDV, SEQ ID. NO. 28; or a functional equivalent thereof;
GRILHNGAY, SEQ ID. NO. 29; or a functional equivalent thereof;
TYLPTNASL, SEQ ID. NO. 30; or a functional equivalent thereof;
EYVNARHCL, SEQ ID. NO. 31; or a functional equivalent thereof;
AYSLTLQGL, SEQ ID. NO. 32; or a functional equivalent thereof;
ALCRWGLLL, SEQ ID. NO. 33; or a functional equivalent thereof;
HLYQGCQV, SEQ ID. NO. 34; or a functional equivalent thereof;
QLRSLTEIL, SEQ ID. NO. 35, or a functional equivalent thereof;
ILHNGAYSL, SEQ ID. NO. 36; or a functional equivalent thereof;
ILLVVVLGV, SEQ ID. NO. 37; or a functional equivalent thereof;
DLTSTVQLV, SEQ ID. NO. 38; or a functional equivalent thereof;
VLVKSPNHV, SEQ ID. NO. 39; or a functional equivalent thereof; and
wherein said polypeptide is not
supported by original claims 1, 9, and 21 and also where we say the full-length HER-2 is not good.

22. (Once Amended) A [The] method of [claim 18] stimulating a response in a subject, comprising: administering [a composition wherein the composition is] a multivalent peptide to said subject; wherein said multivalent peptide [which] comprises

(a) 2 or more HER-2 B cell epitopes, a Th cell epitope, and a template, wherein said two or more HER-2 B cell epitopes are different, and wherein said HER-2 B cell epitopes and said Th cell epitope are attached to said template, or

(b) 2 or more HER-2 CTL epitopes, a Th cell epitope, and a template,wherein said two or more HER 2 CTL-epitopes are different, and wherein said HER-2 CTL epitopes and said Th cell epitope are attached to said template, or

(c) one or more HER-2 B cell epitopes, one or more HER-2 CTL epitope, a Th cell epitope, and a template, wherein said one or more HER-2 B cell epitopes, said one or more HER-2 CTL epitope and said Th cell epitope are attached to said template;

wherein each of said HER-2 B cell epitopes comprises a sequence selected from the group consisting of: .

TGTDMKLRLPASPETHLDM, SEQ ID NO. 1, or a functional equivalent thereof;
AVLDNGDPLNNTTPVTGASPGG, SEQ ID NO. 2, or a functional equivalent thereof;

LWKDIFHKNNQLALTLIDTNRS, SEQ ID NO. 3, or a functional equivalent thereof;
TLIDTNRSRACHPCSPMCKGSRCWGESSEDCQSLT, SEQ ID NO. 4, or a functional equivalent thereof;
ALVTYNTDTFESMPNPEGRYT, SEQ ID NO. 5, or a functional equivalent thereof;
PLHNQEVTAEDGTQRAEKCSKPCA, SEQ ID NO. 6, or a functional equivalent thereof;
PESFDGDPASNTAPLQPE, SEQ ID NO. 7, or a functional equivalent thereof;
LYISAWPDSLPDLSVFQNLQ, SEQ ID NO. 8, or a functional equivalent thereof;
LFRNPHQALLHTANRPEDE, SEQ ID NO. 9, or a functional equivalent thereof;
CLPCHPECQPQNGSVTCFGPEADQCVACAHYKDP, SEQ ID NO. 10, or a functional equivalent thereof;
KPDLSYMPIWKFPDEEGA, SEQ ID NO. 11, or a functional equivalent thereof; and
INGTHSCVDLDDKGCPAEQRAS, SEQ ID NO. 12, or a functional equivalent thereof; and

wherein each of said HER-2 CTL epitopes comprises a sequence selected from the group consisting of:

ILWKDIFHK, SEQ ID. NO. 21; or a functional equivalent thereof;
ILKETELRK, SEQ ID. NO. 22; or a functional equivalent thereof;
VLRENTSPK, SEQ ID. NO. 23; or a functional equivalent thereof;
AARPAGATL, SEQ ID. NO. 24; or a functional equivalent thereof;
LPASPETHL, SEQ ID. NO. 25; or a functional equivalent thereof;
LPTHDPSPL, SEQ ID. NO. 26; or a functional equivalent thereof;
CRWGLLLAL, SEQ ID. NO. 27; or a functional equivalent thereof;
RRFTHQSDV, SEQ ID. NO. 28; or a functional equivalent thereof;
GRILHNGAY, SEQ ID. NO. 29; or a functional equivalent thereof;
TYLPTNASL, SEQ ID. NO. 30; or a functional equivalent thereof;
EYVNARHCL, SEQ ID. NO. 31; or a functional equivalent thereof;
AYSLTLQGL, SEQ ID. NO. 32; or a functional equivalent thereof;
ALCRWGLLL, SEQ ID. NO. 33; or a functional equivalent thereof;
HLYQGCQV, SEQ ID. NO. 34; or a functional equivalent thereof;
QLRSLTEIL, SEQ ID. NO. 35, or a functional equivalent thereof;
ILHNGAYSL, SEQ ID. NO. 36; or a functional equivalent thereof;
ILLVVVLGV, SEQ ID. NO. 37; or a functional equivalent thereof;
DLTSTVQLV, SEQ ID. NO. 38; or a functional equivalent thereof;

VLVKSPNHV, SEQ ID. NO. 39; or a functional equivalent thereof;

KIFGSLAFL, SEQ ID. NO. 40; or a functional equivalent thereof; and

IISAVVGIL, SEQ ID. NO. 41; or a functional equivalent thereof.